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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/687,609	10/13/2000	Roberto Weinmann	BMS-0010	9813

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EXAMINER

CLOW, LORI A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 04/22/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/687,609

Applicant(s)

WEINMANN ET AL.

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 February 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11, 13, 18 and 33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11, 13, 18 and 33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR § 1.821 through 1.825 because on page 26, line 36 of the specification there is a 4 amino acid sequence which does not have a SEQ ID NO. Also, two nucleic acids sequences are set forth in the specification on page 27, lines 11-15, which are not present in the sequence listing. Finally, on page 9, line 27 of the specification, nucleic acid SEQ ID Nos: 1 and 2 are recited. However, in review of the actual sequence listing, these SEQ ID Nos: correspond to amino acid sequences. Applicants are given the same response time regarding this failure to comply as that set forth to respond to this office action. A complete response to this office action includes compliance with this sequence rule compliance requirement. Failure to comply may result in abandonment of this application.

Claim Rejections - 35 USC § 112

Claims 1-10, 11, 13, 18, and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **Written Description** rejection.

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The recited crystal is defined by the coordinates listed in Table A of the specification which includes the Androgen Receptor-Ligand Binding Domain/Androgen Receptor-Ligand Binding Domain ligand (AR-LBD/AR-LBD ligand) complex only. An adequate written description defining other structures, as recited in the claims, is not provided. For example, claim 1 describes a crystal **comprising** AR-LBD and AR-LBD ligand complex. However, the specification describes a crystal containing the coordinates listed in Table A, but does not describe any other crystal. Thus, partial structures, such as the AR-LBD crystal are not described. Also, claim 7 describes a crystal **having** the coordinates listed in Table A, which is also inclusive of structures with coordinates beyond those in Table A.

Claims 1-11, 13, 18, and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a crystal comprising a molecular complex of AR-LBD/AR-LBD ligand as described in Table A, does not reasonably provide enablement for all molecules encompassed by said claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The specification enables the crystal complex defined by Table A, however does not enable the receptor ligand binding domain crystal alone or any of the specified residue fragments as in claims 11, 13, and 18. The crystal structures of claims 2, 3, and 4 are not defined by a SEQ ID NO. and could therefore represent any amino acid sequence. Furthermore, the recited positions of claims 11, 13, and 18 intended to define the structure of the ligand binding domain are only enabled as to the Table A structure. The specific crystal defined by the specification has set coordinates and contains a binding domain that is set. Residues within a given structure can be modified to include any one of the 20 amino acids known and the

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specification does not provide enablement for this vast number of modifications that would ultimately define a crystal other than what is presented in Table A. Because of the vast number of species encompassed by the claimed genus and the lack of guidance as to what structural changes may be made in the amino acid sequence around the active binding domain such that the resulting structure would remain active and structurally sound, it would require undue experimentation to make or use the invention over the entire scope of the claims.

Claim 33 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a crystal of an AR-LBD complex according to Table A, does not reasonably provide enablement for an AR-LBD or an AR-LBD ligand, separately. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The table referred to in the specification is Table A.

The examiner is relying upon the data in Table A to interpret the specification. Therefore, the specification is not enabling for the crystal of AR-LBD alone, but only for AR-LBD/AR-LBD ligand complex according to Table A.

Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **New Matter** rejection.

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Claim 33 is drawn to a crystal comprising an AR-LBD and AR-LBD ligand complex with the Table A coordinates. However, this is not described in the specification as originally filed. Table A contains the atomic coordinates for the AR-LBD complexed with AR-LBD ligand. In the instant case the ligand is dihydrotestosterone (DHT). On page 27, lines 38-47, the crystallization process is described:

The AR-LBD-Dihydrotestosterone (DHT) **complex** was crystallized at 20° C by vapor diffusion in the hanging-drop mode. In the crystallization trials, the **protein complex** as obtained from MMB&B was used without further purification. In the initial trial to obtain crystallization conditions, a sparse matrix crystallization screen was done with the Crystal Screens 1 and 2 (Hampton Research). For each crystallization trial, a 2 μ l drop was prepared by mixing 1 μ l of purified protein (1.9 mg ml⁻¹) with an equal volume of reservoir solution. The reservoir contained 1.0 ml of the precipitating solution. Small crystals were obtained in two days from six of the drops (table 1).

The specification does not contain a written description of a crystal of only AR-LBD and therefore, this claim represents new matter.

Claims 1-11, 13, 18, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear as to what the metes and bounds of the AR-LBD are. Claim 1 only defines the AR-LBD via its name plus some crystal limitations which are not directed specifically to what AR-LBD is. For example, the specification on page 1, lines 23-27, defines the AR-LBD as 261 residues with a molecular weight of 30,245 Da. Claim 2 recites that the AR-LBD should be at least 200 amino acids, claim 3 and 4 recites it as 246 amino acids, and Table A contains residue 672-917, 246 amino acid residues. The specification also defines AR-LBD as having the activity of AR-LBD (see page 5, lines 23-30) and also defines AR-LBD from rat as residues 650-

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902 and AR-LBD from human as residues 666-918, both 253 residue (see specification on page 2, lines 9-11 which cites PNAS (1988) Vol.85, page 7211).

The numbering of the amino acid residues to possibly define AR-LBD is also confusing because the instant specification on page 3, lines 8-10, states that the human numbering system is utilized in the instant disclosure. Consideration of Table A, however, reveals that the first amino acid is Ile numbered as residue 672 and the last is HIS numbered as 917. In the PNAS sequencing article disclosed on page 2, lines 9-11, the human sequence is set forth in Figure 2 on page 7212, including numbering. In the human sequence on said page 7212, the amino acid position at 672 is confusingly Phe and the amino acid at position 917 is Thr, which does not correspond to the instant application numbering in Table A.

As such, claims 1-11, 13, 18, and 33 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the AR-LBD/DHT complex of Table A, does not reasonably provide enablement for a broader element. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. If the activity of the AR-LBD is evaluated in order to enable various AR-LBD types, then the activity assay for such an evaluation is essential subject matter for the practice of these claim embodiments. The instant specification lacks any particular activity assay description and publications incorporated by reference for such activity are improper, but may resolve this issue.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be

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accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10am to 6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

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April 21, 2003

Lori A. Clow, Ph.D.

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Lori A. Clow

Ardin H. Marschel
ARDIN H. MARSCHEL
PRIMARY EXAMINER